IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

TEVA PHARMACEUTICALS USA, INC. and MAYNE PHARMA INTERNATIONAL PTY LTD.,	)	
Plaintiffs/Counterclaim Defendants,	)	C.A. No. 13-2002 (GMS)
v.	)	
FOREST LABORATORIES, INC.,	)	
Defendant/Counterclaim Plaintiff.	)	

FOREST'S RESPONSIVE CLAIM CONSTRUCTION BRIEF

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I. INTRODUCTION

Forest's proposed claim constructions are based on the intrinsic evidence and provide the reasonable certainty required by *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120 (2014). Plaintiffs, in contrast, seek to untether their constructions from the plain meaning of the disputed terms and the intrinsic evidence. Plaintiffs argue for unsupported constructions – many of which would render the claims indefinite – in an attempt to overcome the complete disconnect between the asserted claims and the accused Namenda XR® product. The claims are directed to diminishing or abolishing wind-up pain, but Namenda XR® does not treat wind-up or any other kind of pain. The claims also require an immediate release form of the active ingredient, but Namenda XR® has only extended release pellets. Thus, Namenda XR® is fundamentally different than the claimed methods disclosed in the '000 patent.

Not finding support in the intrinsic evidence for their proposed constructions, Plaintiffs turn instead to extrinsic evidence. Plaintiffs seek to rely on an expert declaration to contradict the intrinsic evidence, including the applicants' own explicit definition of the term "wind-up." Such extrinsic evidence, however, cannot overcome the intrinsic evidence. Furthermore, the deposition testimony of Plaintiffs' expert actually undercuts Plaintiffs' proposed constructions. Forest's proposed claim constructions are rooted firmly in the intrinsic evidence, and hold Plaintiffs to what the applicants actually described and claimed as their alleged invention.

For all these reasons, and the reasons set forth in its opening brief, Forest respectfully requests that the Court adopt its proposed constructions.

II. THE DISPUTED CLAIM TERMS

A. "Wind-Up" – Plaintiffs Cannot Disavow the Explicit Definition of Wind-Up in the '000 Patent and Its File History

'000 Patent: Claims 1, 3, 6, 12		
Claim Term	**Forest's Proposal**	**Plaintiffs' Proposal**
wind-up	Because of the novel requirements for activation, it is believed that the NMDA receptor complex plays only a minor role in routine synaptic transmission. However, the receptor complex may be activated following repeated afferent stimuli as occurs during trauma such as surgery. **Repeated stimuli cause a temporal summation of C-fibre mediated responses of dorsal horn nociceptive neurones; this phenomenon, increased output to a constant input, is known as wind-up.**[1]	an increase in output to a repeated constant input or stimulus, resulting in an exaggerated pain response to a stimulus which normally would not be painful

Plaintiffs' use of Dr. Yaksh's declaration to contradict the definition of "wind-up" set forth in the '000 specification and file history is improper and fails as a matter of law. Extrinsic evidence, such as expert testimony, dictionaries, and learned treatises, cannot be used to contradict the intrinsic evidence. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1317-18 (Fed. Cir. 2005) (*en banc*). Expert testimony, in particular, should be "accorded no weight" when it is "contrary to the meaning shown in the specification." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996). Reliance on expert testimony to contradict a claim term that is clearly and unambiguously defined in the specification is improper. *Id.* at 1584-85; *see also SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187, 1210 (Fed. Cir. 2013) (rejecting expert testimony that was in "conflict with the plain language of the specification").

Forest's proposed construction is taken directly from the '000 patent specification: "Repeated stimuli cause a temporal summation of C-fibre mediated responses of dorsal horn nociceptive neurones; this phenomenon, increased output to a constant input, ***is known as wind-up***." (1:26-29 (emphasis added)). The prosecution history confirms that the phrase "Repeated

[1] To streamline the construction of this claim term, the Court may wish to consider just the final sentence of Forest's proposed construction during the *Markman* process. For that reason, this Responsive Brief focuses on the centrality of the dorsal horn nociceptive neurone activity to the definition of "wind-up" in the '000 patent and its file history.

stimuli cause a temporal summation of C-fibre mediated responses of dorsal horn nociceptive neurones" is integral to the definition of "wind-up." In response to a rejection of the term "diminish or abolish wind up" for indefiniteness under 35 U.S.C. § 112, the applicants represented that the term "wind up" is expressly defined in the specification: "[t]he term 'wind up' is understood by those of ordinary skill in the art ***and is defined on page 1, lines 8-19 of the specification*** [of the pending application, equivalent to column 1, lines 14-29 of the issued '000 patent]." (Tab 2, June 14, 1999 Amendment at 12 (emphasis added)).

Plaintiffs seek to exclude the phrase "Repeated stimuli cause a temporal summation of C-fibre mediated responses of dorsal horn nociceptive neurones," from any construction of the term "wind-up." Tacitly recognizing that the intrinsic evidence does not support their infringement arguments, Plaintiffs have resorted to Dr. Yaksh's declaration. (D.I. 51 at 5-9). Dr. Yaksh's declaration is extrinsic evidence, created for the purpose of this litigation, which cannot overcome the intrinsic evidence in this case. Moreover, Dr. Yaksh's proposed testimony is fundamentally flawed because:

- Dr. Yaksh was not provided with any rules or guidelines regarding what an expert is and is not permitted to do in connection with construing patent claims, or how to treat definitions of words in a patent. (Wilson Decl., Ex. A at 32:18-33:24; 72:3-15).
- Dr. Yaksh did not look at the correct portion of the applicants' prosecution history statement where they identified for the examiner the definition of the term "wind-up," and as such, his declaration was made without reference to the key specification passage. (Wilson Decl., Ex. A at 90:4-92:20; D.I. 52 at ¶ 34).
- Dr. Yaksh improperly relied on extrinsic evidence in his claim construction analysis, in particular the Kristensen article which the applicants did not add to the US specification,

even though it was published by that time and applicants were aware of it, as shown by the applicants' actions before the European Patent Office. (Wilson Decl., Ex. A at 71:4-72:7).[2]

- Dr. Yaksh's declaration indicates that laminectomies are required to assess wind-up in humans, but at his deposition, he admitted that one can assess wind-up in humans without such invasive procedures, and that the Price article does just that. (Wilson Decl., Ex. A at 38:9-39:24; 48:22-50:22).

If anything, the substance of Dr. Yaksh's deposition testimony is fundamentally inconsistent with both (i) Plaintiffs' proposed construction and (ii) Plaintiffs' arguments against Forest's proposed construction. Specifically, Dr. Yaksh admitted that the paragraph the applicants cited as the definition of "wind-up" describes the mechanism of wind-up. (Wilson Decl., Ex. A at 91:8-15). Dr. Yaksh further confirmed that every aspect of Forest's proposed construction is part of that mechanism as he understands it. (*See, e.g.*, Wilson Decl., Ex. A at 64:24-65:11). Dr. Yaksh also admitted that Plaintiffs' proposed construction excludes hyperalgesia, even though the specification clearly includes that as a possible resulting symptom of wind-up. (Wilson Decl., Ex. A at 43:23-46:25). Dr. Yaksh further admitted that he understands wind-up to be a centralized phenomenon caused by repeated painful stimuli which only lasts a few seconds. (Wilson Decl., Ex. A, 25:7-25:23; 75:3-75:12). Dr. Yaksh's description of wind-up as a specific, limited phenomenon stands in sharp contrast with Plaintiffs' broad proposed construction. Plaintiffs' proposed construction would therefore sweep in a wide variety of phenomena that have none of the characteristics that Dr. Yaksh attributed to wind-up, while excluding a

[2] Extrinsic articles and the applicants' statements in a later, European prosecution cannot overcome the plain language of the '000 patent and the U.S. file history – even assuming, *arguendo*, that Plaintiffs' interpretation of those documents is correct. (D.I. 51 at 8-9).

phenomenon that is attributed to wind-up. All of Dr. Yaksh's substantive admissions contradict both Plaintiffs' proposed construction and Plaintiff's arguments against Forest's proposed construction.

Rather than accept the explicit definition of "wind up" provided in the specification, Plaintiffs instead argue about the structure of the sentence at column 1, lines 26-29 of the '000 patent; but this argument is contrary to the grammar, structure, and logic of the entire sentence. (D.I. 51 at 7). Specifically, the phrase "Repeated stimuli cause a temporal summation of C-fibre mediated responses of dorsal horn nociceptive neurones" provides the necessary antecedent for the phrase "this phenomenon." (1:26-29).

Plaintiffs' reliance on portions of the file history to support their proposed construction is similarly unavailing. In passages that Plaintiffs cite, the applicants merely (i) provided additional information regarding what "wind-up" "relates to" and "results in," and (ii) discussed the subjectivity of pain. (D.I. 51 at 5-6). Such explanatory statements in no way contradict or supplant the applicants' express definition of "wind-up," which precedes the portions of the specification on which Plaintiffs attempt to rely. Plaintiffs also quote the examiner's Reasons For Allowance, but the cited passage does not support their construction. There is no evidence that the examiner intended those statements to constitute a formal definition of the term "wind up." (D.I. 51 at 6). And even if the examiner intended to provide a construction of the term, the examiner's statement cannot override the applicants' own express definition.[3]

[3] Plaintiffs cite a case that is totally inapposite to the file history of the '000 patent. (*See* D.I. 51 at 6). In *ACCO*, the court adopted an interpretation not merely because it was in the Reasons for Allowance, but rather because "the examiner's Reasons for Allowance make clear that the examiner and the applicant understood that the invention requires [a certain limitation]." *ACCO Brands, Inc. v. Micro Sec. Devices, Inc.*, 346 F.3d 1075, 1079 (Fed. Cir. 2003). There is no question that the applicants understood "wind-up" to be – in their own words – "defined" by

B. "To Diminish or Abolish Wind-Up" – The Plain Language of the '000 Patent Requires the Treatment to Diminish or Abolish Wind-Up in the Human or Animal Subject of the Administration

'000 Patent: Claims 1, 3, 6, 12		
Claim Term	**Forest's Proposal**	**Plaintiffs' Proposal**
to diminish or abolish wind-up	to diminish or abolish wind-up in the human or animal subject of the administration	No construction is necessary, except for construction of "wind-up."

Forest's proposed construction of the term "to diminish or abolish wind-up" is based on the plain language of the claims and the specification. Every independent claim of the '000 patent includes the phrase "human or animal subject."[4] (Claims 1, 7, 12, and 44). The structure, logic, and grammar of the claims fully support Forest's proposed construction. For example, claim 12 recites: "A method for the treatment of [list of diseases] ***in a human or animal subject***, the method comprising administering ***to the subject*** an effective amount of an analgesic pharmaceutical composition including an NMDA receptor antagonist in an immediate release form combined with an NMDA receptor antagonist in a sustained release form, the immediate release form and sustained release form ***being present in sufficient amounts to diminish or abolish wind-up***." The phrase "human or animal subject" is the antecedent basis for "the subject" to whom the claimed composition is being administered. It would make no sense to interpret the claim to require administering the composition to the subject in an amount sufficient to diminish or abolish wind up in some alternative, unspecified subject. Plaintiffs argue that the applicants would have included the phrase "in the human or animal subject of the administration" at the end of the claims if they meant to tie diminishing or abolishing wind-up to that subject.

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the language that Forest now proposes as its construction for the term. As such, the examiner's statement does not change the express definition of "wind-up" under *ACCO* or any other theory.

[4] Plaintiffs incorrectly suggest that the phrase "human or animal subject" appears only in claim 1, not in claim 12 or elsewhere. (D.I. 51 at 10). At best, Plaintiffs' argument is confusing and does not clearly convey that the phrase "human or animal subject" appears in every independent claim of the '000 patent.

(D.I. 51 at 10). Such language would be completely redundant. Given the overall structure of the claim, it was wholly unnecessary for the applicants to reiterate the phrase "human or animal subject" at the end.

Plaintiffs' argument is also not logical. Plaintiffs' proposed construction would untether the phrase "sufficient amounts to diminish or abolish wind-up" from any point of reference. For example, Plaintiffs' proposed construction would cover administering sufficient amounts to diminish or abolish wind-up in a rat to an adult human subject. There is no support for such a construction in the intrinsic evidence and should be rejected on that basis. Also, Dr. Yaksh admitted that he understands the subject of the study to be an integral part of what it means to diminish or abolish wind-up in the '000 patent. (Wilson Decl., Ex. A at 37:25-38:4).

Finally, Plaintiffs' proposal would render the term "to diminish or abolish wind-up" indefinite. Plaintiff's proposal excludes any reference to the nature of the subject, which is necessary to understand whether a given composition will diminish or abolish windup. As Dr. Yaksh admitted, it is necessary to know the subject to which a composition is administered before one can know if that composition will diminish or abolish wind-up. (Wilson Decl., Ex. A at 77:25-78:18) ("Q: What are the things you would need to know before you could give me a yes or a no answer to whether that substance diminished or abolished wind-up?... Would you need to know the entity you're giving the substance to whether it's cats or humans or some other subject? A: Of course."). Nothing else in the '000 patent clarifies the scope of asserted claims. Indeed, Dr. Yaksh testified that he did not know where the words in the patent claims drew the line with regard to what is needed "to diminish or abolish wind-up." (Wilson Decl., Ex. A at 55:12-56:9). Plaintiffs' proposal gives a person of ordinary skill in the art no guidance with regard to the meaning of the phrase "to diminish or abolish wind-up." Therefore, if Plaintiffs'

proposal prevails, the claims will be rendered indefinite. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120, 2129 (2014) ("a patent's claims [must] inform those skilled in the art about the scope of the invention with reasonable certainty").

C. "For the administration . . . to a Human or Animal Subject for the Treatment of Pain" – The Express Language of the '000 Patent and Its File History Demonstrate that the Preamble to Claim 1 is Limiting and Should Be Given Its Plain Meaning

'000 Patent: Claims 1, 3, 6, 12		
Claim Term	**Forest's Proposal**	**Plaintiffs' Proposal**
for the administration . . . to a human or animal subject for the treatment of pain	to be administered to a human or animal subject for the purpose of preventing, reducing, or relieving pain	No construction is necessary.

1. The Preamble to Claim 1 is Limiting

As set forth in Forest's Opening Brief, the intrinsic evidence fully supports the conclusion that the Claim 1 preamble is limiting. The Claim 1 preamble includes the terms "analgesic pharmaceutical composition" and "for the treatment of pain," concepts that are central to the claimed invention. Indeed, every aspect of the '000 patent is directed towards pain relief. The specification repeatedly emphasizes the analgesic properties of the claimed invention: "[t]he present invention relates to pharmaceutical compositions and is particularly concerned with pharmaceutical compositions containing N-methyl-D-aspartate (NMDA) receptor antagonists ***and their use in the treatment of pain***" (1:7-10); "[t]he composition of the invention i***s suitable for the treatment of chronic or acute pain***," (2:10-11); "the present invention further provides a method for the therapeutic or prophylactic ***treatment of pain in a human or animal subject***" (2:14- 16); "[t]he method of the invention may be used to ***treat chronic or acute pain***" (2:18-19); "[t]he composition of the invention may be used in the ***pre-emptive treatment of pain***" (2:20-21). Each and every independent claim includes limitations directed to "sufficient amounts ***to***

diminish or abolish wind-up" – and even Plaintiffs' proposed constructions acknowledge that "wind-up" is a pain phenomenon.[5] (Claims 1, 7, 12, and 44; D.I. 51 at 4). Forest's proposal stays true to the claim language and aligns with the patent's explicit description in the specification, a description which Plaintiffs assiduously ignore. As the Federal Circuit has emphasized, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *See, e.g., Ormco Corp. v. Align Tech., Inc.*, 498 F.3d 1307, 1313 (Fed. Cir. 2007) (citations omitted).

Moreover, the preamble language "for the administration of an NMDA receptor antagonist to a human or animal subject" is necessary to provide antecedent basis for the claim language requiring sufficient amounts of components "to diminish or abolish wind-up." Without that point of reference from the preamble, there is no way to know what amounts will "diminish or abolish wind-up" – an amount that will necessarily change depending on the nature of the subject to whom the compound is to be administered. As such, the preamble language must be limiting. *See, e.g., Proveris Scientific Corp. v. Innovasystems, Inc.*, 739 F.3d 1367, 1372 (Fed. Cir. 2014) (finding a preamble limiting where the body of the claim "rel[ied] upon and derive[ed] antecedent basis from the preamble").[6]

Plaintiffs also argue that the specification describes "the present invention" without any reference to treatment of pain or analgesia. (D.I. 51 at 12). In fact, the very first use of the term "the present invention" in the specification emphasizes that the '000 patent ***is*** concerned with

[5] As the Court stated in its Order on Forest's Motion to Dismiss under Rule 12(c), "[t]o be sure, pain treatment and wind up figure prominently in the '000 Patent claims." (*See* D.I. 53 at n. 1).

[6] Plaintiffs' incorrect assertion that the recited steps in the body of the claim define a complete method fails for the same reason. (*See* D.I. 51 at 12). There is simply no reference point to evaluate the claim without the preamble. And contrary to Plaintiffs' argument, there is no reason to expect that the dependent claims would necessarily refer back to the preamble merely because the preamble is limiting. (*Id.*)

pain relief: "***The present invention*** relates to pharmaceutical compositions and ***is particularly concerned with*** pharmaceutical compositions containing N-methyl-D-aspartate (NMDA) receptor antagonists and ***their use in the treatment of pain***." (1:6-10 (emphasis added)). Furthermore, the '000 patent states that "[t]he composition of the invention is suitable for the treatment of chronic or acute pain, for example to be administered pre-operatively." (2:10-11). As such, a composition that is not suitable for the treatment of chronic or acute pain ***is not the composition of the invention***. Plaintiffs' argument that most of the specification is without reference to the treatment of pain ignores these express disclosures throughout the specification, which emphasize that the treatment of pain is central to the claimed invention. (D.I. 51 at 12). Plaintiffs cannot ignore the '000 patent's unmistakable disclosure directed specifically to compositions and methods for pain relief.

Plaintiffs argue that the language related to pain relief is permissive rather than mandatory, and cite to the phrase "may be used to treat chronic or acute pain" in the '000 patent. (D.I. 51 at 12). But this language is fully consistent with the remainder of the specification. To the extent the '000 patent describes alternatives to the treatment of chronic or acute pain, those alternatives are also directed to pain management. For example, the specification teaches that "[t]he composition of the invention may be used in the pre-emptive treatment of pain." (D.I. 51 at 12; 2:20-21). Thus, in addition to chronic and acute pain, the '000 patent describes the use of the disclosed compositions in alternative scenarios that are also pain-related.

Plaintiffs argue that the specification teaches using the compositions for purposes other than the treatment of pain. (D.I. 51 at 12). That is incorrect. Plaintiffs cite to a general statement from the "Background of the Invention," noting that NMDA receptor antagonists have been indicated to be effective in the treatment of several conditions. (D.I. 51 at 12; 1:52-63).

Nowhere in the "Invention" section does the '000 patent mention any of these conditions – unlike the alleviation of pain, which is mentioned repeatedly. (Cols. 1-16). Nor does the specification anywhere teach or even describe using "the resulting compositions" for purposes other than pain relief. There is no written support for such non-pain related use anywhere in the '000 patent. Indeed, the only other reference to the conditions cited in the Background of the Invention is in claim 12, which explicitly and repeatedly ties the claimed invention to pain relief:

> "12. A method for the treatment of Huntington's disease amyotrophic lateral sclerosis (ALS), AIDS-related dementia, Alzheimer's disease, schizophrenia, motoneurone diseases and CNS and brain injuries resulting from a number of causes including trauma, stroke and neurosurgery in a human or animal subject,
>
> the method comprising administering to the subject ***an effective amount of an analgesic pharmaceutical composition*** including an NMDA receptor antagonist in an immediate release form combined with an NMDA receptor antagonist in a sustained release form,
>
> the immediate release form and sustained release form being ***present in sufficient amounts to diminish or abolish wind-up***." (Emphasis added).

Plaintiffs also incorrectly state that only some claims are directed to methods for the treatment of pain. (D.I. 51 at 12). In fact, each and every independent claim in the '000 patent is expressly directed to certain dosages present in "sufficient amounts to diminish or abolish wind-up." (Claims 1, 7, 12, and 44). Plaintiffs acknowledge that wind-up is a pain phenomenon. (*See, e.g.*, D.I. 51 at 4, Plaintiffs' proposed construction). Thus, contrary to Plaintiffs' argument, all claims of the '000 patent require dosages sufficient to diminish or abolish a particular kind of pain. (D.I. 51 at 4). Plaintiffs' arguments regarding claims 1 and 12 are particularly implausible, given that those claims are expressly directed to "the treatment of pain" and "an effective amount of an analgesic," respectively.

None of Plaintiffs' citations to the file history contradict the disclosure in the specification of the '000 patent and the plain language of the asserted claims, discussed above. (D.I. 51 at 13).

In fact, the file history further demonstrates the centrality of pain relief to the '000 patent. Specifically, during prosecution, the applicants distinguished their invention over the Chow patent on the grounds that the prior art did not address a method of treatment for pain related to wind-up. (Tab 2, June 14, 1999 Amendment at 12). The applicants further stated, regarding the Chow patent, "[n]or does the reference show or suggest the use of a immediate and controlled release form in the treatment of the specific condition." (*Id.*). This concept of treating pain is precisely the concept embodied in the Claim 1 preamble, and is a limitation that the applicants relied on to distinguish the prior art during prosecution.

2. The Claim 1 Preamble Should Be Afforded Its Plain Meaning

As set forth in its Opening Brief, Forest's proposed construction of the claim 1 preamble embodies the plain meaning of the claim language and is supported by the intrinsic evidence. Plaintiffs' argument to the contrary ignores the plain language of the claim and specification. (D.I. 51 at 14).

D. "Immediate Release Form" / "Immediate Release" – Plaintiffs' Proposed Construction Is Inconsistent with the Specification and Would Render the Claims Indefinite

'000 Patent: Claims 1, 3, 6, 12		
Claim Term	**Forest's Proposal**	**Plaintiffs' Proposal**
immediate release form	pharmaceutical form in which the release of the active ingredient is not delayed and/or extended	a form that releases the active ingredient promptly after administration
immediate release	release that is not delayed and/or extended	release the active ingredient promptly after administration

Forest's proposed construction is firmly grounded in the plain meaning of the claim language and the intrinsic evidence. Throughout the specification, the patentees describe the immediate release form as a form where nothing has been done to alter or extend the release of the active ingredient. For example, the specification states that "[a] suitable immediate release (IR) form of the NMDA receptor antagonist may simply be particles of the antagonist or

particles of the antagonist admixed with soluble components . . . ." (3:29-32). The specification further discloses that "the IR cores may be coated with a rapidly disintegrating or dissolving coat for aesthetic, handling, or stability purposes." (6:11-13). The specification also states that the immediate release form "may simply be particles of the antagonist or the antagonist deposited on a core." (8:50-52).

Plaintiffs' use of the vague and relative term "promptly" not only seeks to blur the clear distinction between immediate release and sustained release, but also renders the asserted claims indefinite. (D.I. 51 at 14). Plaintiffs' proposed constructions would not inform a person of ordinary skill in the art about the scope of the invention with reasonable certainty. The person of ordinary skill would not understand how "promptly" the formulation must release the active ingredient to be considered "immediate release" under Plaintiffs' proposed constructions. Plaintiffs' proposals would also create the anomalous result that an active ingredient that is slow to dissolve in the body would not be deemed immediate release, even if nothing is done to change its release profile.

Plaintiffs point to the specification's citation of Pharmacopeia XXII in an unavailing attempt to support their use of the word "promptly" in their proposed constructions. (D.I. 51 at 15). But Plaintiffs' argument takes the word "promptly" out of its proper context in the specification. The specification states: "A controlled-release dosage form as defined in US Pharmacopoeia XXII includes extended release dosage forms which allow at least a twofold reduction in dosing frequency as compared to the drug presented as a conventional dosage form and ***delayed release dosage forms*** which release the drug at a time other than ***promptly*** after administration." (3:55-60). The word "promptly" here is used to explain a delayed release

dosage form, which only begins to release the active ingredient after the passage of some time interval following administration.

Plaintiffs argue that Forest's proposed construction is somehow improper because the specification teaches that the immediate release form may be coated or otherwise delay release. (D.I. 51 at 16). This argument is not supported by the intrinsic evidence. For example, the '000 patent states: "Alternatively the IR cores may be coated with a rapidly disintegrating or dissolving coat for aesthetic, handling, or stability purposes." (6:10-13). The '000 patent makes clear that such coatings or other ingredients, which may in some circumstances incidentally prolong the release of the active, nonetheless do not constitute "delay and/or extension" in any meaningful sense.[7]

E. "Sustained Release Form" / "Sustained Release" – Plaintiffs' Proposed Construction Is Inconsistent with the Specification and Would Render the Claims Indefinite

'000 Patent: Claims 1, 3, 6, 12		
Claim Term	**Forest's Proposal**	**Plaintiffs' Proposal**
sustained release form	pharmaceutical form in which the release of the active ingredient is delayed and/or extended	a form that releases the active ingredient over a period of time that is longer than that of the immediate release form
sustained release	release that is delayed and/or extended	release the active ingredient over a period of time that is longer than that of the immediate release form

[7] Plaintiffs cite to cases that (i) interpret claim limitations that are different from any at issue here, (ii) concern other patents, and (iii) have claim construction holdings different from the construction that Plaintiffs propose in this case. (D.I. 51 at 17). For example, *UCB, Inc. v. Mallinckrodt Inc.*, C.A. No. 12-463-LPS, 2013 U.S. Dist. LEXIS 103955, at *12-13 (D. Del. July 25, 2013), considered the limitations "immediate release bead" and "extended release bead" from U.S. Patent No. 6,344,215, titled "Methylphenidate modified release formulations." The court ultimately held that "immediate release bead" means "a bead that delivers a portion of the total amount of [API] for rapid onset of action," and "extended release bead" means "a bead that delivers a portion of total amount of [API] in a controlled manner over an extended period of time." *Id.* Not only do these constructions differ from Plaintiffs' proposed constructions, they are in fact closer to Forest's proposed constructions.

As explained in its Opening Brief, Forest's proposed constructions of "sustained release form" and "sustained release" are supported by the plain meaning of the claim language and the specification. Throughout the specification, the patentees describe the sustained release form as a form in which something has been done to alter and extend the release of the active ingredient. For example, the specification states that "[p]referably, the controlled release component is a sustained (or extended) release form." (4:6-7). The specification discloses that "[a] suitable sustained release (SR) form of the NMDA receptor antagonist may be a matrix tablet composition." (4:9-10). The '000 patent examples also support Forest's proposed construction. Example 2 discloses a theoretical product having "an immediate release component of 30% and a sustained release of the other 70% over approximately a 12 hour period at intestinal pH." (14:57-59). Similarly, Example 3 discloses a formulation in which the "sustained release portion released 13% at 2 hours in pH 1.2 dissolution media, showing that the capsule does not dose dump in the stomach." (16:29-31).

Plaintiffs seek to erase the clear teaching of the '000 patent that immediate and sustained release forms are distinct from each other. For example, Plaintiffs' proposed construction of "sustained release" would cover any form that releases ***any amount of time*** – however small – after an immediate release form would release. Plaintiffs point to several portions of the specification in support of their position, but never articulate how these citations support Plaintiffs' proposed constructions. (D.I. 51 at 18). Plaintiffs argue that "[t]he specification does not define the sustained release as having any particular release profile," but then note that the specification teaches a sustained release form with a therapeutic effect that preferably extends "over a period greater than about 6 hours," "with 8 to 24 hours being especially preferred." (D.I. 51 at 18). In no way do references to 6, 8, or 24 hours support Plaintiffs' construction, which

would consider a form that releases the active over ***any amount of time*** longer than an immediate release form to be a sustained release form. Moreover, Plaintiffs' proposed construction essentially asks the Court to construe "delayed release" as any form that releases the active ingredient "***not promptly*** after administration," or "***just after promptly*** after administration." This again fails to inform a person of ordinary skill in the art about the scope of the invention with reasonable certainty.

Finally, Plaintiffs' proposed definition is inconsistent with the specification because in some circumstances it treats substances identified only as suitable for "immediate release" forms as "sustained release" forms. Specifically, the '000 patent includes certain components on the list of substances suitable for immediate release forms which it omits from its list of substances suitable for sustained release forms. (3:29-52). In this way, certain components are only identified as suitable for immediate release forms, such as the surfactants sodium lauryl sulfate and chremophor. (*Id.*). Under Plaintiffs' proposed construction, any form with a release profile longer than the fastest immediate release composition is a "sustained release form" – even if that composition is made up of excipients that the '000 patent discloses as suitable only for immediate release forms. Moreover, Plaintiffs' discussion underscores that their proposed constructions would render the claims indefinite. Given their argument that the '000 patent "does not define the sustained release as having any particular release profile," a construction of "sustained release" as merely "longer than that of the immediate release form" would give a person of ordinary skill in the art no clear guidelines as to what constitutes an immediate release form and what constitutes a sustained release form.

F. "The Immediate Release Form and Sustained Release Form Being Present in Sufficient Amounts" – The Plain Language of the '000 Patent Requires that Immediate Release Form and the Sustained Release Form Each Must Be Present in Sufficient Amounts to Diminish or Abolish Wind-Up

'000 Patent: Claims 1, 3, 6, 12		
Claim Term	**Forest's Proposal**	**Plaintiffs' Proposal**
the immediate release form and sustained release form being present in sufficient amounts	the immediate release form and the sustained release form each being present in a sufficient amount	collectively, the immediate release form and sustained release form contain sufficient amounts

Forest's proposed construction embodies the plain language of the term and is wholly consistent with the specification. The claim language expressly states that the immediate release form and the sustained release form must be present in "sufficient ***amounts***" to diminish or abolish wind up. (Claim 1 (emphasis added)). The use of the plural form, "amounts," confirms that the limitation requires that each of the immediate and sustained release forms be present in an amount that, on its own, is sufficient to diminish or abolish wind up. This construction is consistent with the purpose of the invention, in that an immediate release dosage that is not present in a sufficient amount to diminish wind-up would do nothing to provide immediate relief – which would defeat the purpose of an immediate release component for the treatment of pain.[8]

The applicants' arguments during the prosecution of the European counterpart to the '000 patent are consistent with the plain language of the claim. There, the applicants argued that the "immediate and sustained release forms must be present ***in sufficient amounts*** to achieve the desired effect to diminish or abolish wind up." (Tab 3, March 8, 2002 Response at 2 (emphasis

[8] Plaintiffs argue that it is "illogical" to interpret the claims to require an immediate release form sufficient to diminish or abolish wind-up, plus an additional amount of NMDA receptor antagonist in sustained release form sufficient to diminish or abolish wind-up. (D.I. at 19). Plaintiffs' argument is inconsistent with the disclosures of the '000 patent – the objective of which is to provide immediate pain relief with the immediate release component and then longer-term pain relief over time with the sustained release component. (3:55-60; 9:13-17; 10:27-30).

added)). The applicants further argued that "it is directly and unambiguously derivable from the disclosure of the application as filed that ***the active ingredients are to be present in sufficient amounts***." (*Id*. (emphasis added)). The plural nature of the phrase "active ingredients" shows that the applicants intended there to be enough of each form to have an effect on wind-up. *See, e.g.*, U.S. Food and Drug Administration, "Drugs@FDA Glossary of Terms," available at: http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm ("Active Ingredient - An active ingredient is any component that provides pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or animals."). The applicants' European admissions are especially relevant, as the disclosures for "sufficient amounts" are the same across the prosecutions. Thus, the European prosecution confirms that Forest's construction is correct.[9]

Plaintiffs impermissibly seek to import the word "collectively" into the asserted claims. But importing this additional term "collectively" contradicts the plain language, grammar, and structure of the claims. (D.I. 51 at 18). If the two forms were to be considered "collectively," they would constitute "a sufficient amount" – not "sufficient amounts." *See, e.g., Source Vagabond Systems Ltd. v. Hydrapak, Inc.*, 753 F.3d 1291, 1299-1300 (Fed. Cir. 2014) (explaining that "[i]nstead of looking to the words themselves, [the patentee] added language without support from the specification or prosecution history, altering otherwise unambiguous claim language, a practice this court has repeatedly rejected").

The portions of the specification that Plaintiffs rely on do not support their proposed construction. (D.I. 51 at 19). For example, Plaintiffs cite to a portion of the specification stating

[9] The Court has discretion to consider the applicants' European statement when construing the claims. *See, e.g., Starhome GmbH v. AT & T Mobility LLC*, 743 F.3d 849, 858 (Fed. Cir. 2014) (holding that statements made before foreign patent offices can be relevant to interpreting the claims).

that according to the invention, the immediate release and sustained release forms are combined into a single dosage. (D.I. 51 at 19). But the specification goes on to say that the proper range for the immediate release form is approximately 5% to 90% of the composition, preferably 10% to 60%. (2:46-49). If Plaintiffs' interpretation were correct, there would be no reason to specify a minimum immediate release percentage, so long as the aggregate combined dosage were reached. Therefore, Plaintiffs' own citation contradicts their proposed claim construction.

Plaintiffs also argue that, if Forest's proposed construction were correct, dependent claims 13, 14, and 15 would have specified the amount of active ingredient in each of the forms, rather than in the aggregate. (D.I. 51 at 19). This argument is unavailing. The '000 patent teaches that a given aggregate dosage may support a range of immediate release to sustained release dosage ratios. (2:46-51). There is nothing inconsistent with the language of the independent claims. In this case, the dependent claims recite an aggregate dosage, without further restricting the claims to a particular ratio or range of immediate release form to sustained release form.

Plaintiffs' argument based on Example 2, which discusses a dose of 200 mg per day of the claimed composition, is similarly untenable. (D.I. 51 at 19-20). Example 2 discloses that 60 mg of the 200 mg dose is present in the immediate release form and the remaining 140 mg is present in the sustained release form. Plaintiffs argue that because 60 mg and 140 mg of amantadine are purportedly each less than the "therapeutic amount" of 200 mg, all that matters is the aggregate value. (D.I. 51 at 20). ***But the phrase "therapeutic amount" does not appear in the '000 patent, and is neither what is claimed nor what Example 2 teaches***. In fact, Example 2 teaches that 200 mg is the "normal dosing regimen" of amantadine, given in "two divided doses of 100 mg." (D.I. 51 at 20). There is nothing in the '000 patent to suggest that this 200 mg "normal dosing regimen" is the lowest dosage that can "diminish or abolish wind-up," as the

claims require. (Cols. 14-16). Therefore, there is nothing in Example 2 to suggest that the disclosed amounts of immediate release and sustained release forms are not each sufficient to diminish or abolish wind up over distinct time periods. Example 2 is wholly consistent with Forest's proposed construction.

Plaintiffs' proposed construction is driven by their infringement contentions. Plaintiffs seek to expand the scope of the claims so that an extended release composition would meet the term "immediate release form" if just one extended release drug pellet inadvertently received less extended release coating than the others. But that is not what the applicants described throughout the specification and prosecution history as the allegedly unique features of the disclosed compositions having both immediate release and sustained release forms "present in sufficient amounts" to diminish or abolish wind-up. Even if a few pellets in a Namenda XR® capsule inadvertently have less extended release coating than others, they would be in such a small amount that they would not provide any independent activity, unlike the immediate release form of the asserted claims. Accordingly, Plaintiffs' proposal should be rejected. *See, e.g.*, *Ormco* at 1313 ("The construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction.").

III. CONCLUSION

For all these reasons, Forest respectfully requests that the Court adopt its proposed constructions for the claim terms in dispute.

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April 24, 2015

CERTIFICATE OF SERVICE

I hereby certify that on March 4, 2015, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on March 4, 2015, upon the following in the manner indicated:

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